

Original Article



Long-Term Oncological Outcomes of Reduced Three-Port Laparoscopic Gastrectomy for Early-Stage Gastric Carcinoma: a Retrospective Large-Scale Multi-Institutional Study

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ABSTRACT

Purpose: With advances in surgical techniques, reduced-port laparoscopic surgery is increasingly being performed for the treatment of gastric carcinoma. Many studies have reported satisfactory short-term outcomes after reduced 3-port laparoscopic gastrectomy (LG). The aim of this study was to investigate the long-term oncological outcomes of 3-port LG in patients with gastric carcinoma.

Materials and Methods: We reviewed the medical records of 1,117 patients who underwent LG for gastric carcinoma in three major institutions between 2012 and 2015. The data showed that 460 patients underwent 3-port LG without assistance, and 657 underwent conventional 5-port LG. We compared the overall and disease-free survival rates between the 2 groups.

Results: There were 642 male and 475 female patients with a mean age of 56.1 years. Among them, 1,028 (92.0%) underwent distal gastrectomy and 89 (8.0%) underwent total gastrectomy. In the final pathologic examination, 1,027 patients (91.9%) were stage I, 73 (6.5%) were stage II, and 17 (1.5%) were stage III, and there were no significant difference in the pathologic stage between groups. The 3- and 5-port LG groups showed no significant differences in the 5-year overall survival (94.3% vs. 96.7%, $P=0.138$) or disease-free survival (94.3% vs. 95.9%, $P=0.231$). Stratified analyses according to pT and pN stages also showed no significant differences in overall or disease-free survival between the two groups.

Conclusions: Long-term survival after 3- and 5-port LG was comparable in patients with early-stage gastric carcinoma. The 3-port technique requiring limited surgical assistance may be an appropriate surgical option for this patient population.

Keywords: Gastrectomy; Laparoscopy; Reduced port surgery; Stomach neoplasm; Survival

INTRODUCTION

Since its introduction in the early 1990s, laparoscopic gastrectomy (LG) has been rapidly adopted for the treatment of gastric carcinoma [1]. Several studies have demonstrated the

Author Contributions

Conceptualization: L.H.H., J.O., L.J.H.; Data curation: L.H.H., J.O., L.J.H.; Formal analysis: L.H.H., J.O., L.J.H.; Funding acquisition: L.H.H.; Investigation: L.H.H., J.O., L.J.H.; Methodology: L.H.H., J.O., L.J.H.; Project administration: L.H.H., J.O., L.J.H.; Resources: L.H.H., J.O., S.H.H., C.M.G., R.S.Y., S.T.S., B.J.M., K.S., L.J.H.; Supervision: L.H.H., J.O., L.J.H.; Validation: L.H.H., J.O., L.J.H.; Visualization: L.H.H., J.O.; Writing - original draft: L.H.H., J.O.; Writing - review & editing: L.H.H., J.O., L.J.H.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

clinical benefits of LG over open surgery, such as faster bowel recovery, shorter hospital stay, and fewer postoperative complications [2,3]. Conventional LG techniques use five or more abdominal ports and require a surgical team that consists of a surgeon, assistant, and scopist. With advances in surgical techniques and instruments, experienced gastric surgeons have developed reduced-port LG, a procedure in which fewer abdominal ports are required, reducing the need for surgical assistance. Previous studies have reported short-term outcomes of reduced-port LG, demonstrating its technical feasibility and safety [4]. Reduced-port LG is also accepted as a useful approach to confront the lack of surgical assistance, especially in small health centers [5].

Single-port LG for gastric cancer was first reported by Omori et al. [6] in 2011. It is performed via a single umbilical incision using a specially designed multichannel port. This technique is demanding even for skilled surgeons because of the operative difficulties caused by handling all instruments through a single channel. Therefore, some surgeons sought to overcome the technical difficulties of single-port LGs by adding additional ports [7,8]. Unlike conventional 5-port LGs, 3-port LGs use two operator ports and one umbilical port. Because this technique uses 2 operator ports and does not require specialized instruments, it can be easily adopted by gastric surgeons who are familiar with conventional LGs [9]. Three-port LG is also called “duet-LG,” emphasizing the fact that it is performed by a surgeon and scopist alone [10]. Several studies have reported the technical feasibility and safety of 3-port LG compared with those of conventional 5-port LG [9-13]. However, the long-term oncological outcomes of 3-port LG have rarely been investigated. In this study, we investigated the long-term oncological outcomes of 3-port LG in a large cohort of patients from multiple institutions.

MATERIALS AND METHODS

Patients

Using institutional gastric cancer databases, we reviewed the records of patients who underwent LG for gastric carcinoma in three major institutions (Samsung Medical Center, Chonnam National University Hwasun Hospital, and Seoul St. Mary's Hospital) in South Korea between January 2012 and December 2015. We excluded patients with other organ malignancies to exclude possible effects on long-term outcomes. A total of 1,117 patients were enrolled, of whom 460 underwent 3-port LG and 657 underwent conventional 5-port LG. The indications for laparoscopic surgery were the same in each institution and included cT1N0 tumors on preoperative staging. The decision regarding 3-port vs. conventional 5-port LG was made by the patient or patient's representative after being informed of the operative procedures. This study was approved by the institutional review boards of each institution, which waived the requirement for informed consent from patients.

Data collection and definition

Clinicopathological data were collected from prospectively constructed databases in each institution. Demographic data included age, sex, body mass index (BMI), and American Society of Anesthesiology (ASA) physical status. Operation data included the extent of gastric resection, reconstruction, operating time, operative blood loss, and need for blood transfusion. Pathological data included tumor size, histological type, resection margin, number of retrieved lymph nodes, and pTNM stage based on the seventh edition of the American Joint Cancer Committee TNM classification [14]. Postoperative outcomes included morbidity, mortality, and hospital stay length. Postoperative morbidity and mortality were defined as any complications

or deaths within 30 days after surgery. The severity of the complications was classified according to the Clavien–Dindo classification of surgical complications [15].

The primary outcomes of this study were overall survival (OS) and disease-free survival (DFS). OS was defined as the time from surgery to death from any cause. DFS was defined as the time from surgery to death or disease recurrence. After surgery, patients were regularly followed up using abdominal computed tomography (CT) and endoscopic evaluations every 6 or 12 months during the subsequent 5 years. Additional work-ups, such as chest CT, liver magnetic resonance imaging, and positron emission tomography/CT, were performed as appropriate. Adjuvant chemotherapy using oral fluoropyrimidine (S-1) or capecitabine plus oxaliplatin was administered to patients with pathologic stage \geq II. The survival status of all patients was ascertained using registration data from the Korea National Statistical Office and medical records. The median follow-up period was 48 months (range, 1–67 months).

Operative techniques

The details of the operative technique of 3-port LG have been described in previous reports [9,10]. Briefly, the patient was placed in the reverse Trendelenburg position. One camera port and two operator ports were made in the umbilicus and on the right and left side of the patient. The operation was performed with no assistance. The operative techniques, including gastric resection and lymph node dissection, were performed as in conventional LG, following the principles of gastric cancer treatment guidelines [16,17]. D1+ lymph node dissection (LND) was performed for cT1N0 tumors. All reconstructions were performed intracorporeally, and the choice of reconstruction was decided at the discretion of the surgeon.

In conventional LG, five abdominal ports, including two operator ports, two assistant ports, and one umbilical port for the laparoscope, were used. The operative techniques, including gastric resection and LND, were the same as those for 3-port LG, and the operation was performed with assistance.

Statistical analyses

Student's *t*-test was used to compare continuous variables, and the χ^2 test or Fisher's exact test was used to compare categorical variables, as appropriate. Patient survival was analyzed using the Kaplan–Meier method and compared using the log-rank test. Multivariate survival analyses were performed using the Cox proportional hazards model. All statistical analyses were performed using SPSS ver. 19.0 software (SPSS Inc., Chicago, IL, USA), and a *P*-value <0.05 was considered statistically significant.

RESULTS

Patient characteristics

Table 1 presents the clinicopathological characteristics of patients. There were no significant differences in age, sex, or ASA status between the two groups; however, the mean BMI was higher in the 3-port LG group (23.4 vs. 22.8 kg/m², *P*=0.001). Tumor size, histologic type, and Lauren classification did not significantly differ between the two groups. The mean numbers of retrieved lymph nodes in the 3- and 5-port LG groups were 39±14 and 40±13, respectively (*P*=0.177). In the final pathologic examination, 1027 patients (91.9%) were stage I, 73 patients (6.5%) were stage II, and 17 patients (1.5%) were stage III; there were no significant differences in the final pathologic stage between the two groups.

Table 1. Clinicopathological characteristics

Characteristics	Three-port LG (n=460)	Five-port LG (n=657)	P-value
Age (yr)	55.8±12.3	56.4±12.4	0.498
Sex			0.075
Male	279 (60.7)	363 (55.3)	
Female	181 (39.3)	294 (44.7)	
Body mass index (kg/m ²)	23.4±3.1	22.8±2.8	0.001
ASA classification			0.496
1	226 (49.1)	307 (46.7)	
≥2	234 (50.9)	350 (53.3)	
Tumor size (cm)	2.7±1.6	2.7±1.6	0.920
Proximal margin (cm)	4.2±2.7	4.8±2.9	0.002
No. retrieved lymph nodes	39±14	40±13	0.177
Histologic type			0.194
Papillary	10 (2.2)	20 (3)	
Well differentiated	183 (39.8)	280 (42.6)	
Moderately differentiated	119 (25.9)	190 (28.9)	
Poorly differentiated	128 (27.8)	149 (22.7)	
Mucinous	2 (0.4)	2 (0.3)	
Signet ring cell	18 (3.9)	16 (2.4)	
Lauren classification			0.590
Intestinal	180 (39.1)	254 (38.7)	
Diffuse	204 (44.3)	282 (42.9)	
Mixed	66 (14.3)	111 (16.9)	
Unclassified	10 (2.2)	10 (1.5)	
Lymphovascular invasion	70 (15.2)	75 (11.4)	0.063
Tumor invasion (pT)*			0.836
T1	419 (91.1)	597 (90.9)	
T2	26 (5.7)	34 (5.2)	
T3	12 (2.6)	18 (2.7)	
T4a	3 (0.7)	8 (1.2)	
Nodal metastasis (pN)*			0.886
N0	408 (88.7)	591 (90)	
N1	31 (6.7)	41 (6.2)	
N2	10 (2.2)	14 (2.1)	
N3a	8 (1.7)	7 (1.1)	
N3b	3 (0.7)	4 (0.6)	
TNM stage*			0.936
IA	386 (83.9)	555 (84.5)	
IB	36 (7.8)	50 (7.6)	
IIA	18 (3.9)	23 (3.5)	
IIB	12 (2.6)	20 (3.0)	
IIIA	6 (1.3)	5 (0.8)	
IIIB	2 (0.4)	4 (0.6)	

Data are expressed as mean±standard deviation or number (%).

LG = laparoscopic gastrectomy; ASA = American Society of Anesthesiologists.

*Seventh edition of the AJCC TNM classification.

The operative results are shown in **Table 2**. Among the 1117 patients, 1028 (92.0%) underwent distal gastrectomy and 89 (8.0%) underwent total gastrectomy; there was no significant difference in the extent of gastric resection between the two groups. Billroth II anastomosis was more frequently performed in the 3-port LG group (54.1% vs. 33.2%, $P<0.001$). All patients underwent laparoscopic surgery without open conversion. No patients in the 3-port LG group required conversion to 5-port surgery. There were no significant differences with respect to operative outcomes, including operating time, operative blood loss, or need for blood transfusion between the two groups. Postoperative morbidity, mortality, and hospital stay did not significantly differ between the two groups.

Table 2. Operative outcomes in the two groups

Variables	Three-port LG (n=460)	Five-port LG (n=657)	P-value
Extent of gastric resection			
Distal	421 (91.5)	607 (92.4)	0.598
Total	39 (8.5)	50 (7.6)	
Reconstruction			
Billroth I	164 (35.7)	367 (55.9)	<0.001
Billroth II	249 (54.1)	218 (33.2)	
Roux-en Y	47 (10.2)	72 (11.0)	
Operating time (min)	150.8±43.9	148.5±43.9	0.384
Operative blood loss (mL)	105.8±138.1	93.8±75.6	0.091
Blood transfusion	9 (2.0)	9 (1.4)	0.443
Morbidity	70 (15.2)	66 (10.0)	0.134
≥Grade III complications	24 (5.2)	19 (2.9)	0.057
Mortality	1 (0.2)	2 (0.3)	0.755
Hospital stay (days)	9.4±5.2	9.2±2.4	0.340

Data are expressed as mean±standard deviation or number (%).
LG = laparoscopic gastrectomy.

Long-term survival

Fig. 1 shows the Kaplan–Meier survival curves of the 3- and 5-port LG groups. The 5-year OS rates of the 3- and 5-port LG groups were 94.3% and 96.7%, respectively ($P=0.138$, **Fig. 1A**). The hazard ratio of 3-port LG for OS was 1.61 (95% confidence interval [CI] = 0.853–3.03). The 5-year DFS of the 3- and 5-port LG groups were 94.3% and 95.9%, respectively ($P=0.231$, **Fig. 1B**). The hazard ratio of 3-port LG for DFS was 1.42 (95% CI, 0.80–2.52). When adjusting for other clinicopathological factors, including sex, age, ASA classification, extent of gastric resection, histological type, lymphovascular invasion, and pathological stage, the adjusted hazard ratios of 3-port LG for OS and DFS were 1.55 (95% CI, 0.81–2.99) and 1.54 (95% CI, 0.57–4.18), respectively.

Fig. 2 shows the survival curves of the 3-port and conventional 5-port LG groups at different pathological stages. There were no significant differences in overall survival between the two groups in stage I ($P=0.425$, **Fig. 2A**) and stage II–III patients ($P=0.419$, **Fig. 2B**). Likewise, DFS did not significantly differ between the two groups for stage I ($P=0.479$, **Fig. 2C**) and stage II–III patients ($P=0.599$, **Fig. 2D**).

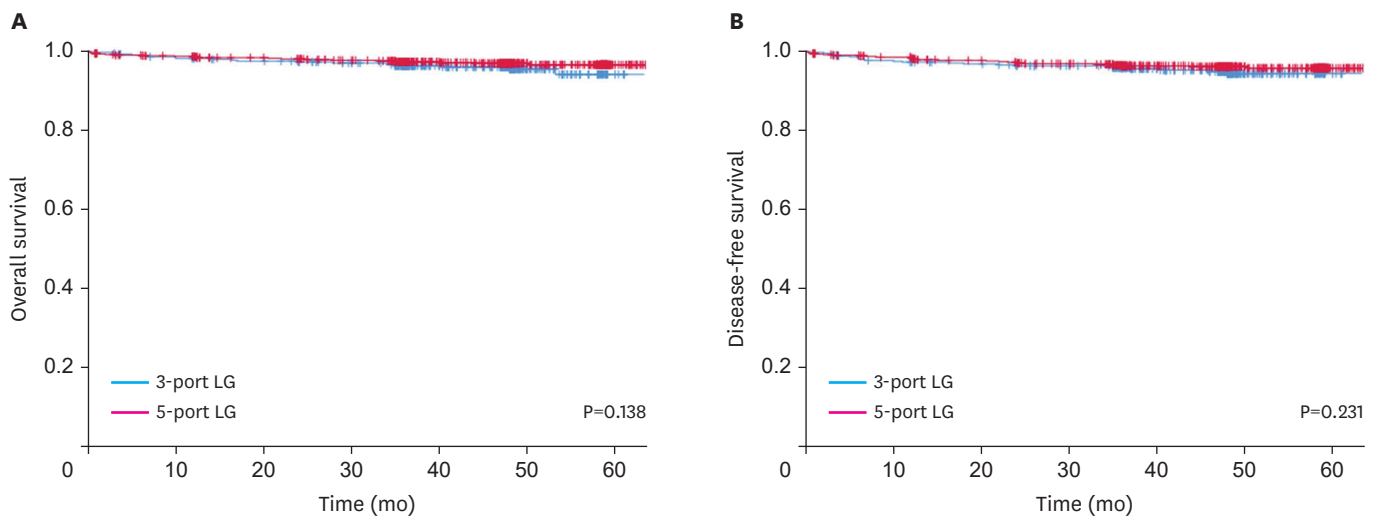


Fig. 1. Kaplan–Meier survival curves for the 3- and 5-port LG groups. (A) Overall survival and (B) disease-free survival. LG = laparoscopic gastrectomy.

Three-port Laparoscopic Gastrectomy

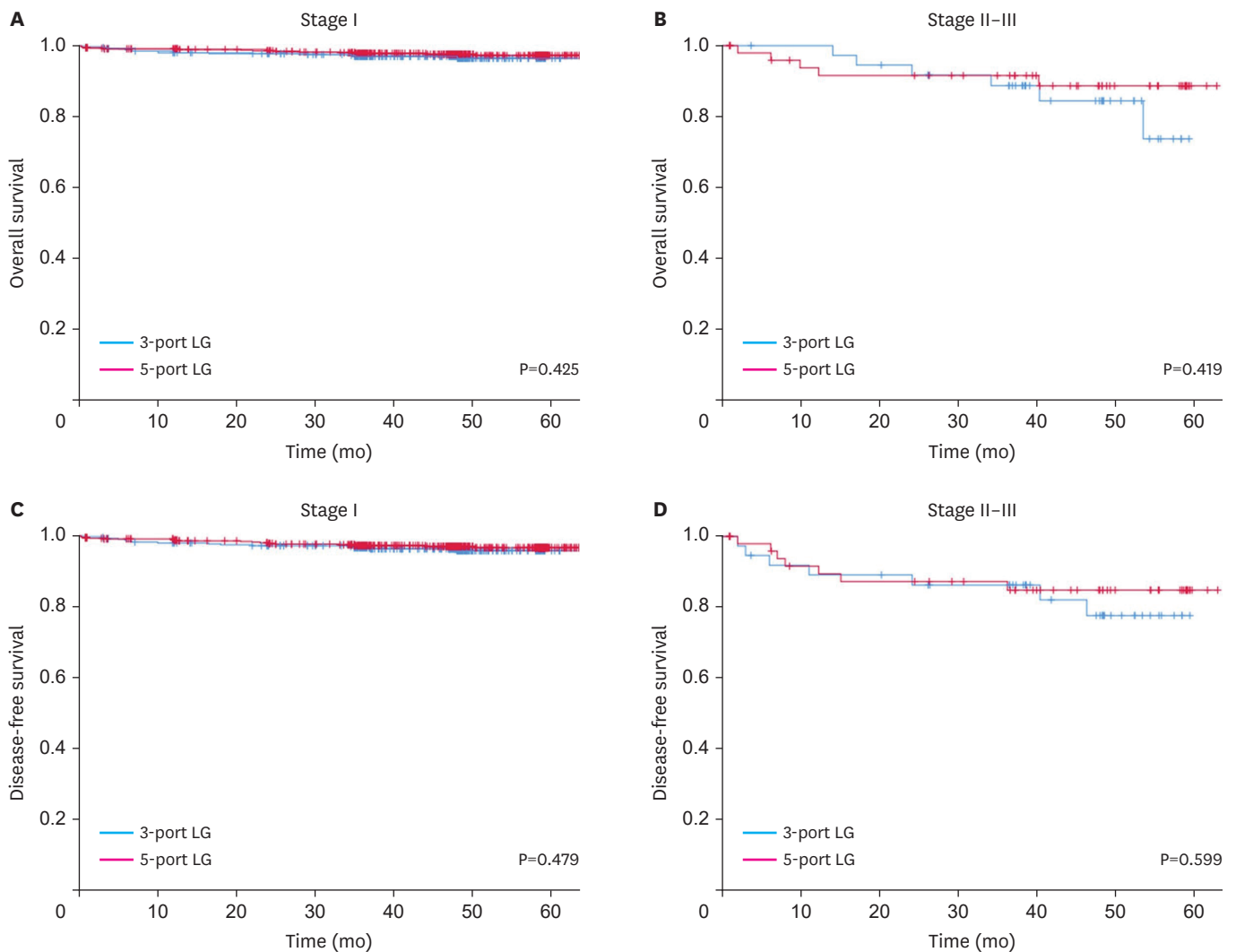


Fig. 2. Kaplan-Meier survival curves for patients with different pathologic stages in the 3- and 5-port LG groups. (A) Overall survival in stage I, (B) overall survival in stage II-III, (C) disease-free survival in stage I, and (D) disease-free survival in stage II-III. LG = laparoscopic gastrectomy.

Fig. 3 shows a forest plot of the hazard ratio of the 3-port LG subgroups according to different clinicopathological factors. There were no significant differences in survival between 3- and 5-port LG for all considered subgroups.

DISCUSSION

Following advances in surgical techniques and instruments, gastric surgeons with vast experience in laparoscopy have introduced reduced-port LG for the treatment of gastric cancer. The initial reports mostly demonstrated the technical feasibility and safety of reduced-port LG compared with those of conventional LG [9-13]. However, the long-term oncological outcomes of reduced-port LGs have not been sufficiently investigated. This is the first study to investigate the long-term oncological outcomes of 3-port LG for gastric carcinoma; the results suggest that long-term survival after 3-port LG is comparable to that after conventional 5-port LG in patients with early-stage gastric carcinoma.

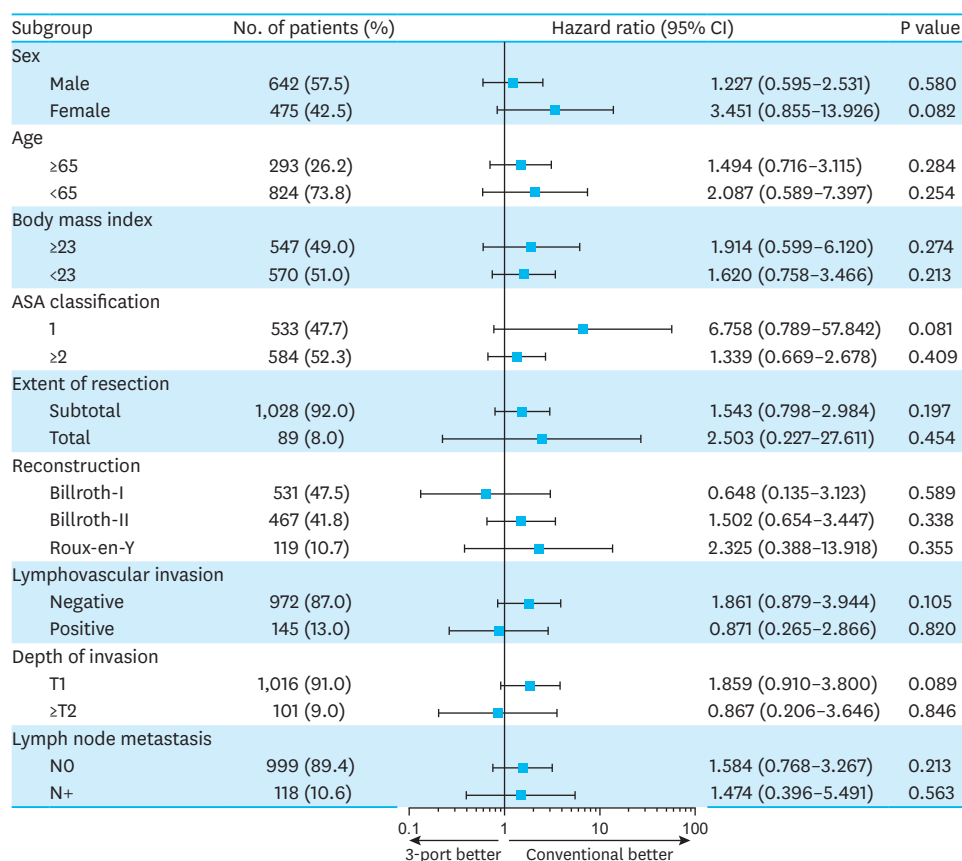


Fig. 3. Forest plot of subgroup analyses. Bars represent hazard ratios with 95% CI of the effect of 3-port laparoscopic gastrectomy on overall survival. CI = confidence interval.

In 2011, Omori et al. [6] first introduced the so-called transumbilical “single-incision” laparoscopic distal gastrectomy. In their technique, they used three working ports through a single 2.5-cm umbilical incision. Later on, various types of multi-channel ports began to be used in this procedure, and “single-port” LG became a common name [18,19]. Some experts have demonstrated the technical feasibility and safety of single-port LG [18-20]. However, single-port LG has not gained wide popularity among gastric surgeons because of the substantial technical difficulties experienced when manipulating multiple instruments through a single umbilical channel. In addition, the merits of single-port LG in improving minimal invasiveness were not significant. In one study that compared single-port and 3-port LG, single-port LG did not improve outcomes in terms of operative blood loss, postoperative pain, morbidity, or hospital stay length [21]. To overcome these technical difficulties, most gastric surgeons agree that additional ports should be inserted if necessary. However, the optimal number of ports in reduced-port LGs remains to be established.

Three-port LG has several advantages over other reduced-port techniques. First, unlike single-port LG, 3-port LG does not require specialized devices, such as a multi-channel port, flexible laparoscope, or curved instruments. Second, by using two operator ports, 3-port LG is free from the operative difficulties of single-port LG, such as loss of triangulation, conflict of instruments, and parallel laparoscopic view. Lastly, the operative techniques of 3-port LG are nearly the same as those of conventional LG, except for some technical tips to overcome

the lack of surgical assistance. Previous studies have shown that gastric surgeons who are familiar with conventional LG can easily perform 3-port LG without increasing the risk for patients [5,9,22].

In addition to technical issues, the oncological safety of reduced-port LG has been a major concern. To date, only a few studies have reported the long-term outcomes of reduced-port LG for gastric carcinoma. Kunisaki et al. [23] compared the long-term survival of dual-port LG (including distal and total gastrectomy) with that of conventional LG in a propensity score-matched cohort. In their study, most patients had early-stage gastric carcinoma, and the two procedures did not show significant differences in overall or relapse-free survival. Our study investigated the long-term survival of 3-port LG in a large cohort of patients from multiple institutions. We found that the long-term survival of patients with early-stage gastric carcinoma treated with 3-port LG was comparable to that of patients treated with conventional 5-port LG. Furthermore, 3-port LG did not increase operative risks, such as morbidity or mortality.

Although the present study suggests the feasibility of adopting 3-port LG for the treatment of early-stage gastric carcinoma, application of reduced-port LG for advanced gastric carcinoma is questionable. Currently, laparoscopic surgery is only indicated for early-stage gastric carcinomas [17]. Likewise, 3-port LG in this study was indicated for patients with early-stage gastric carcinoma (cT1N0) as identified in preoperative staging. Most previous studies, including ours, have demonstrated the technical feasibility and safety of reduced-port LG when performing limited LND for early-stage gastric carcinoma [9-12]. Therefore, this study does not provide useful information about the advantages of reduced-port LG for advanced gastric carcinoma. Recently, some experts have reported techniques for D2 LND using reduced-port LG [20,24]. However, this may only be applicable to surgeons with sufficient knowledge and experience in LG because of the complexity of the extended LND. Therefore, further studies are needed to determine whether 3-port LG can be applied to patients with stage II/III disease.

Although the effect of reducing the number of ports could be trivial in terms of improving the minimal invasiveness of LG, previous studies have reported decreased operative blood loss [5,20,25], less postoperative pain [20], earlier postoperative oral intake [5,20], and shorter hospital stay [20] when using reduced-port LG. However, these results are all derived from small, single-institution studies and need to be verified in large randomized trials. In fact, one of the main reasons for adopting 3-port LG is to perform LG without assistance, as the lack of a surgical resident and assistant has become a practical problem in many institutions. In the present study, we demonstrated comparable short-term surgical outcomes between the two procedures, despite the lack of a surgical assistant during 3-port LG. The clinical benefits of reduced-port LG include diverse aspects, not just measurable surgical outcomes.

Our study had a few limitations. First, although it was a large multi-institutional study, an inherent selection bias is inevitable because of the retrospective study design. However, patient characteristics, including pathological stage, were comparable between the two groups. Second, this study was performed in large health centers, and all participating surgeons were highly skilled gastric surgeons with substantial LG experience. In other words, the surgeons' learning curve for reduced-port laparoscopic surgery was not considered in our study. This may limit the generalizability of our results. A large multi-institutional clinical trial, including small and large hospitals, is required to solve this problem.

In conclusion, this large multi-institutional study demonstrated that long-term oncological outcomes of 3-port LG were comparable to those of conventional 5-port LG in patients with early-stage gastric carcinoma. We believe that 3-port LG may be an appropriate option to perform LG without a surgical assistant, without increasing the risk for patients. Due to the retrospective nature of this study, large randomized clinical trials are warranted to determine the clinical benefits of 3-port LG in treating gastric carcinoma.

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